

Coarse Graining data-driven cellular models in multiscale simulations

Scott L. Diamond, PhD

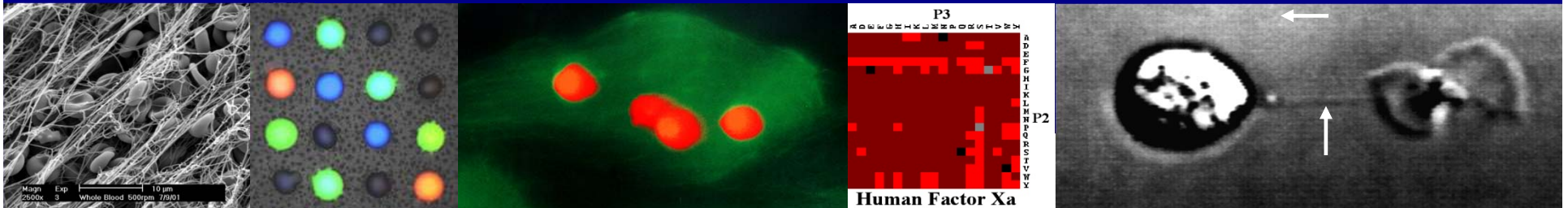
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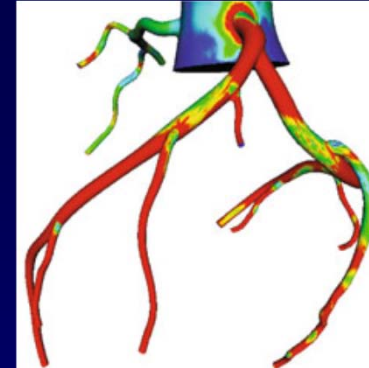
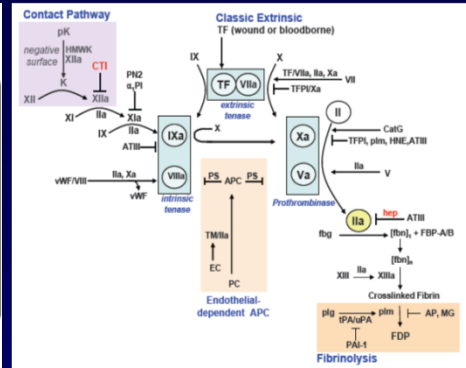
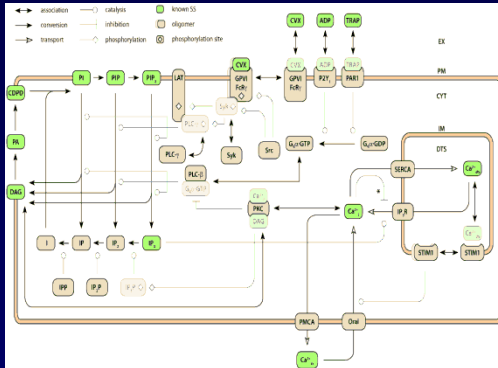
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www.BloodSystemsBiology.org



Blood Systems Biology



Physics
diffusion
velocity
pressure
bond strengths
VWF mechanics
geometry

C. Taylor Lab (Stanford)

Parameters

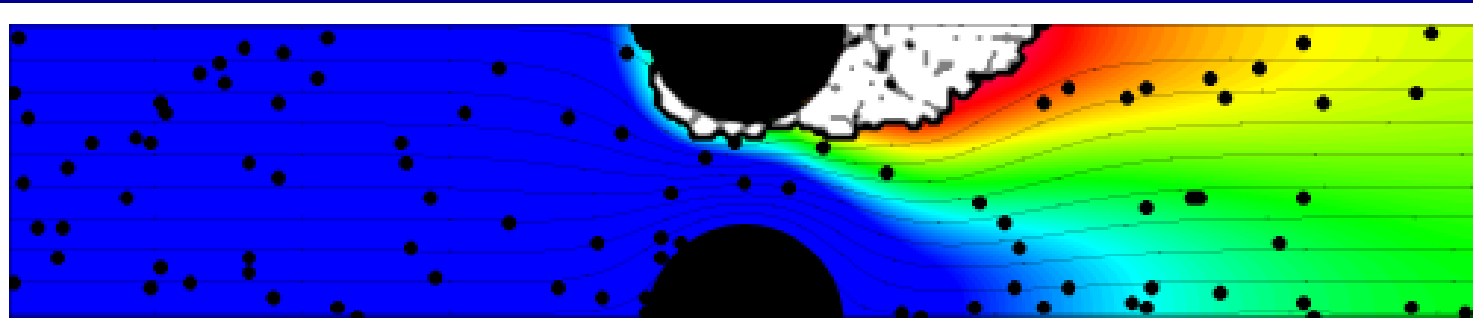
kinetic constants k_i
initial conditions $c_i(0)$

Topology

interaction networks
- nodes and linkages
reaction type

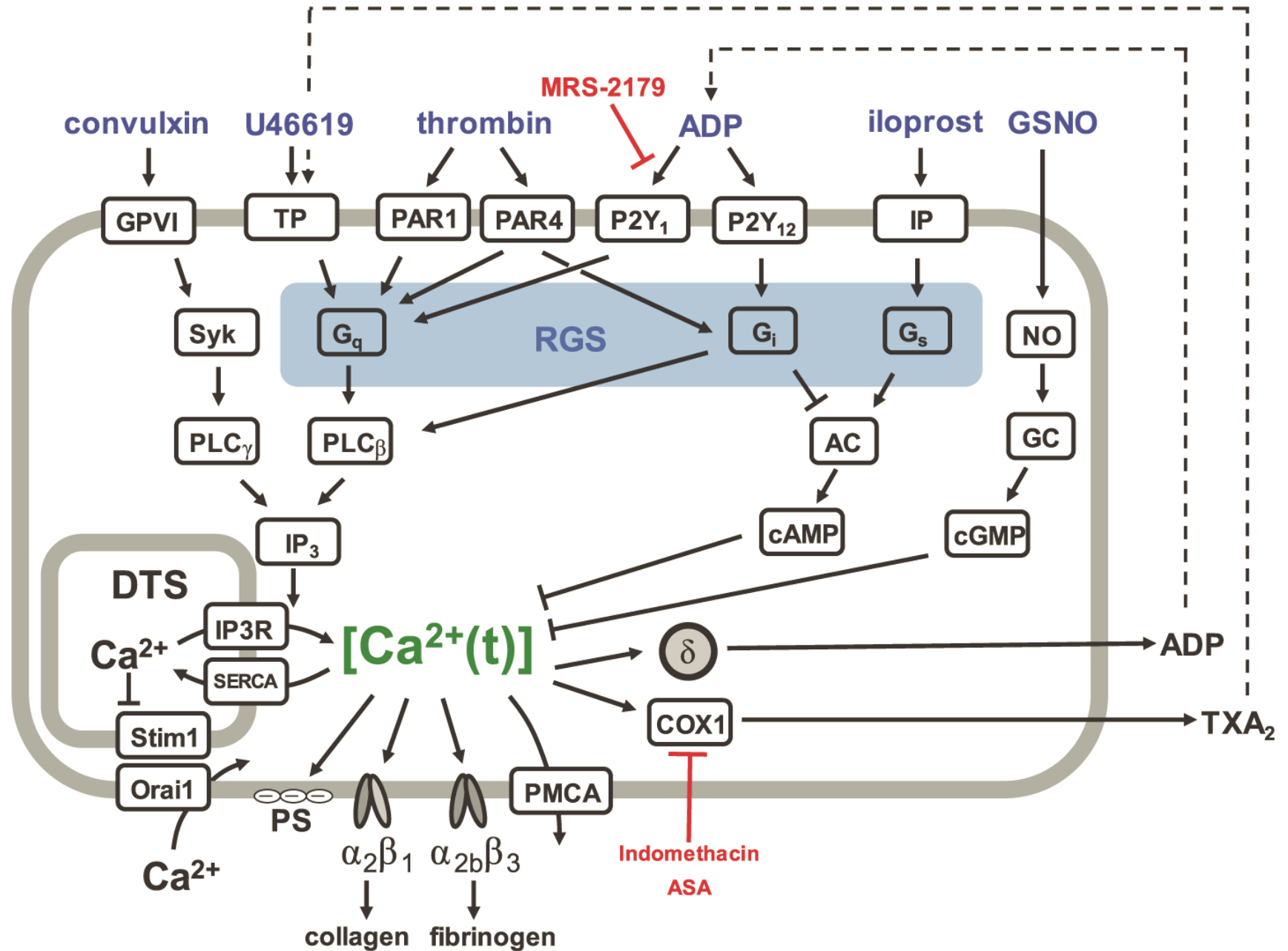
Numerics:

CFD/LB
NN/ODE
LKMC/PDE

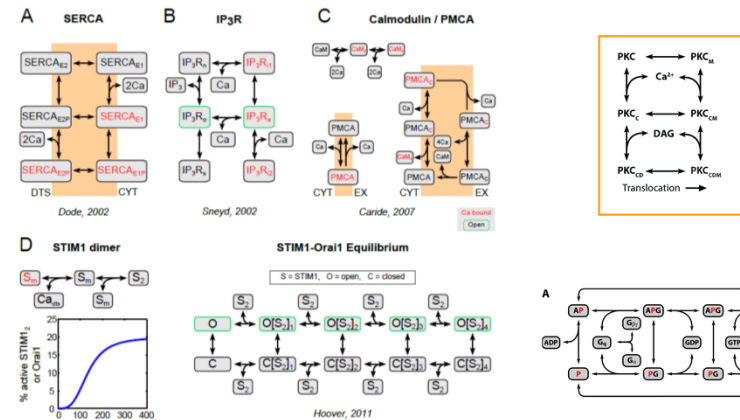


Predictions: System evolution $C_i(x,y,z,t)$

Signaling pathways converging on calcium mobilization

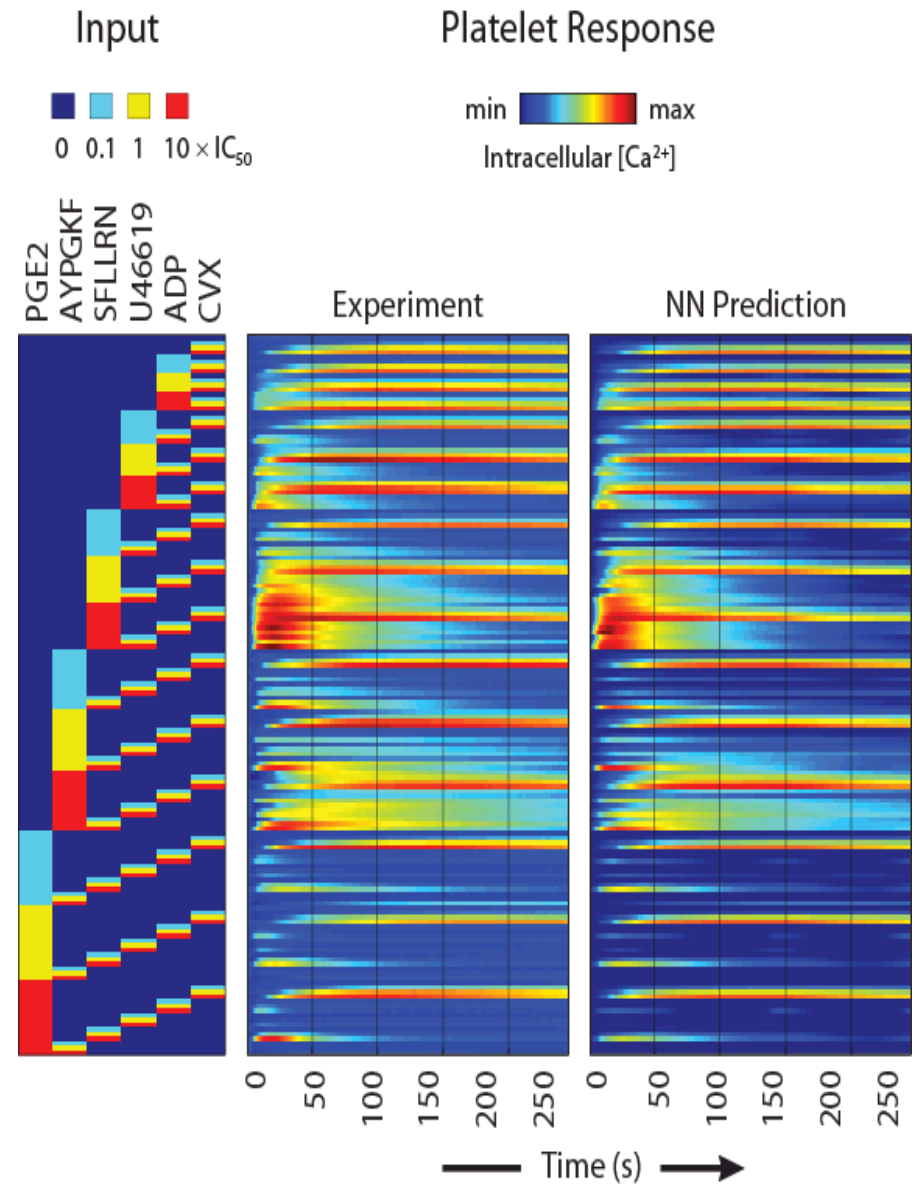
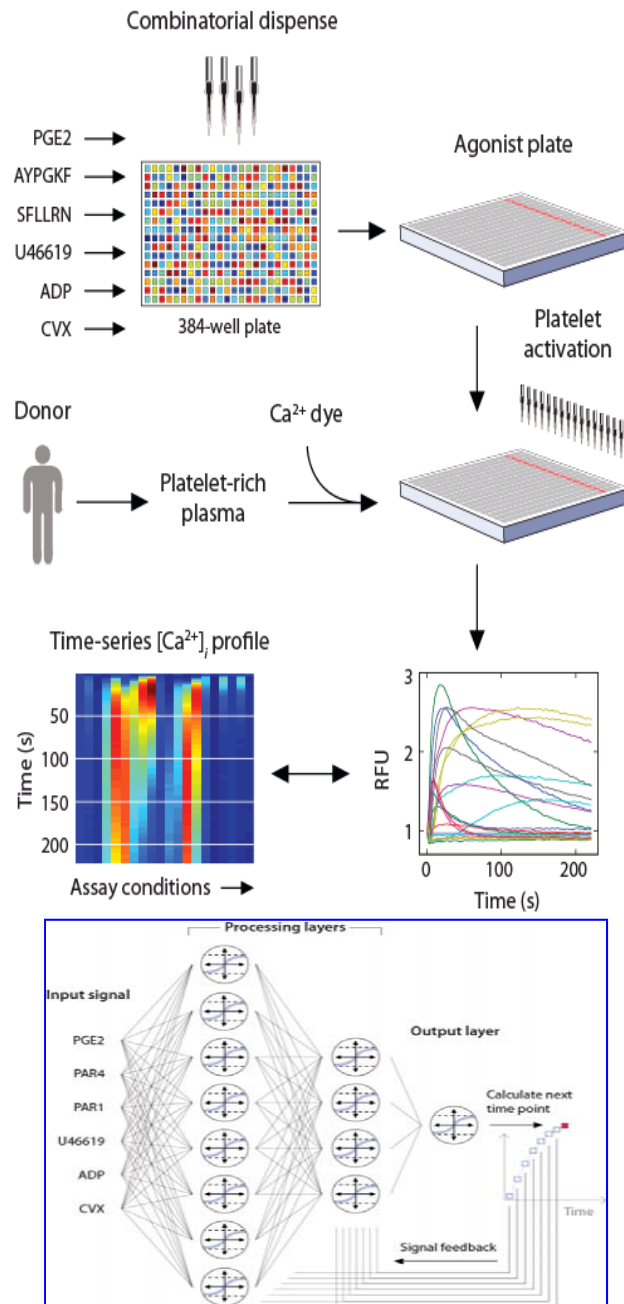


The diagram illustrates the signaling pathways for various platelet receptors. At the top, receptors are shown: GPVI (activated by CVX), TP (activated by U46619), PAR4 (activated by AYPGKF), PAR1 (activated by SFLLRN), P2Y₁ and P2Y₁₂ (activated by ADP), and EP1-4 and IP (activated by PGE₂). These receptors are coupled to G-proteins: GPVI to FcRγ, which then activates Syk and PLC-γ; TP, PAR4, and PAR1 to G_q; P2Y₁ and P2Y₁₂ to G_i; and EP1-4 and IP to G_s. G_q activates PLC-β, which produces IP₃, leading to Ca²⁺ release. G_i inhibits AC, while G_s activates AC. AC produces cAMP, which inhibits Ca²⁺ release. The diagram uses orange shaded boxes to highlight the G_q, PLC-β, and IP₃/Ca²⁺ components.

[illegible][illegible]

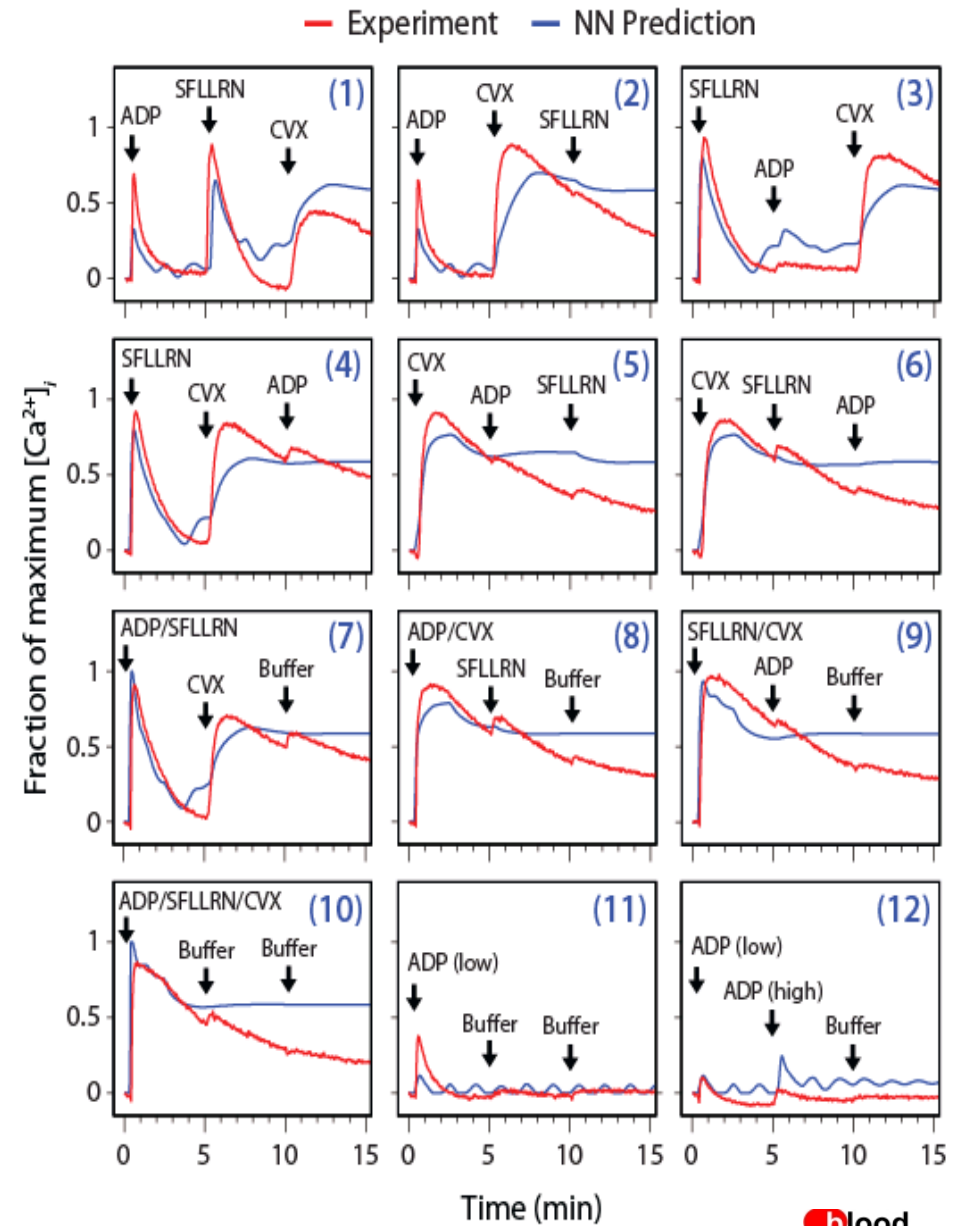
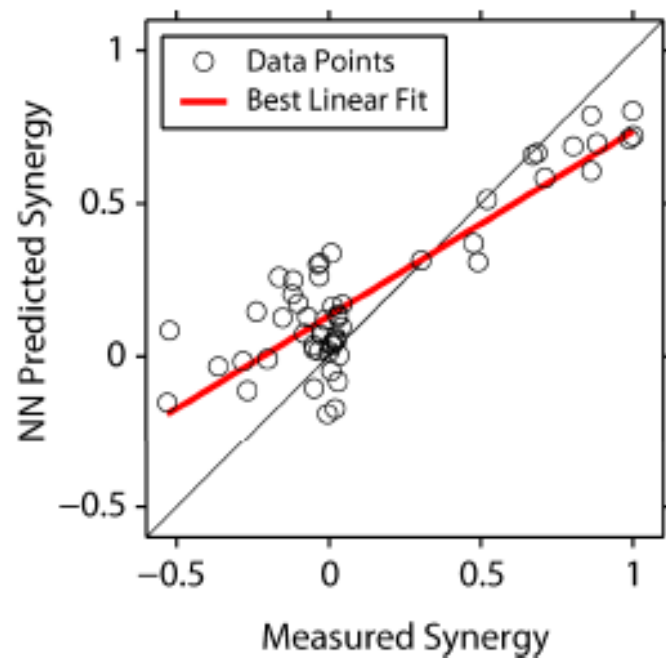
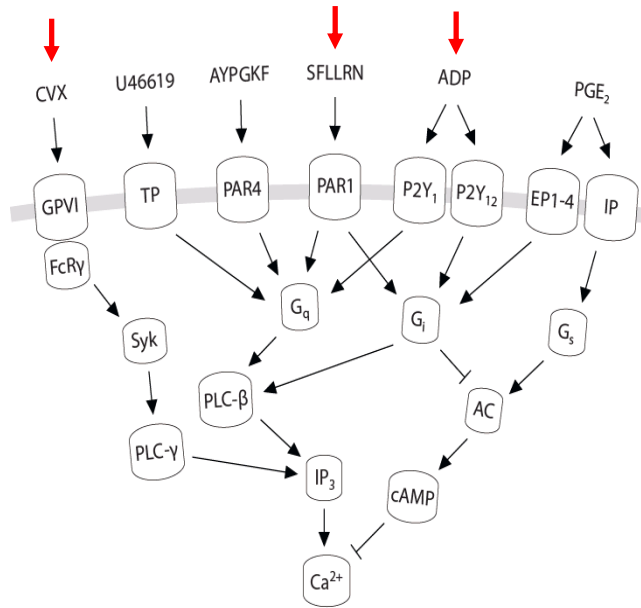
Purvis, et al. *Blood* 2008
Purvis, et al. *PLoS Comp Biol.* 2009
Dolan & Diamond, *Biophys. J.* 2014

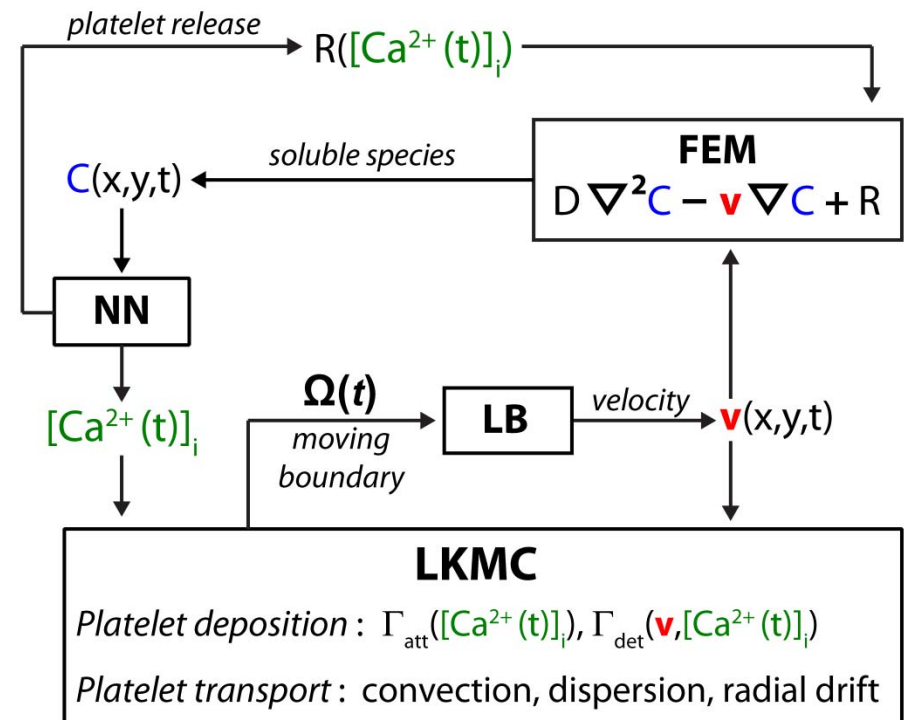
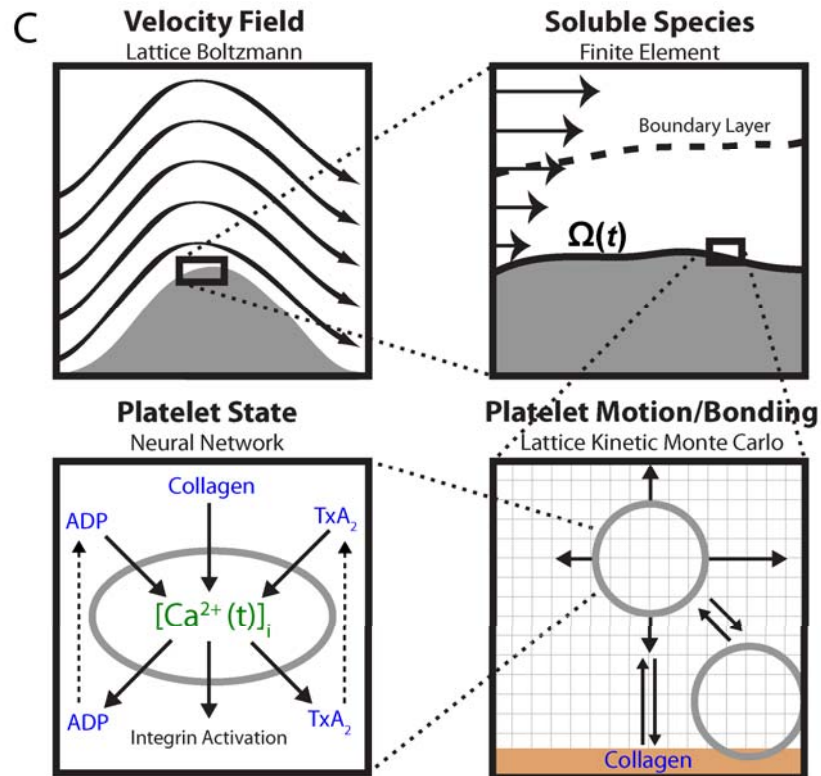
Pairwise Agonist Scanning (PAS)



Chatterjee, et al. *Nature Biotechnology* 2010

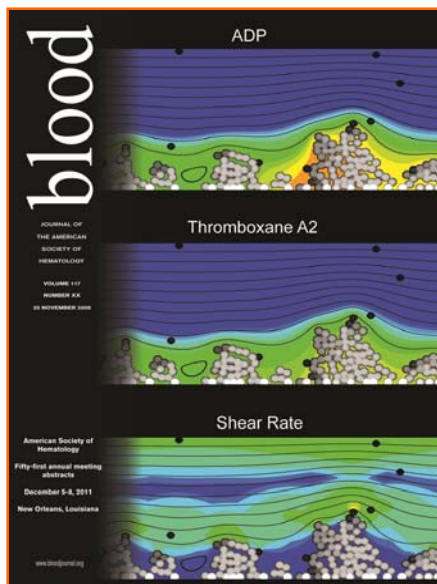
Sequential and ternary addition of: SFFRN, CVX, ADP



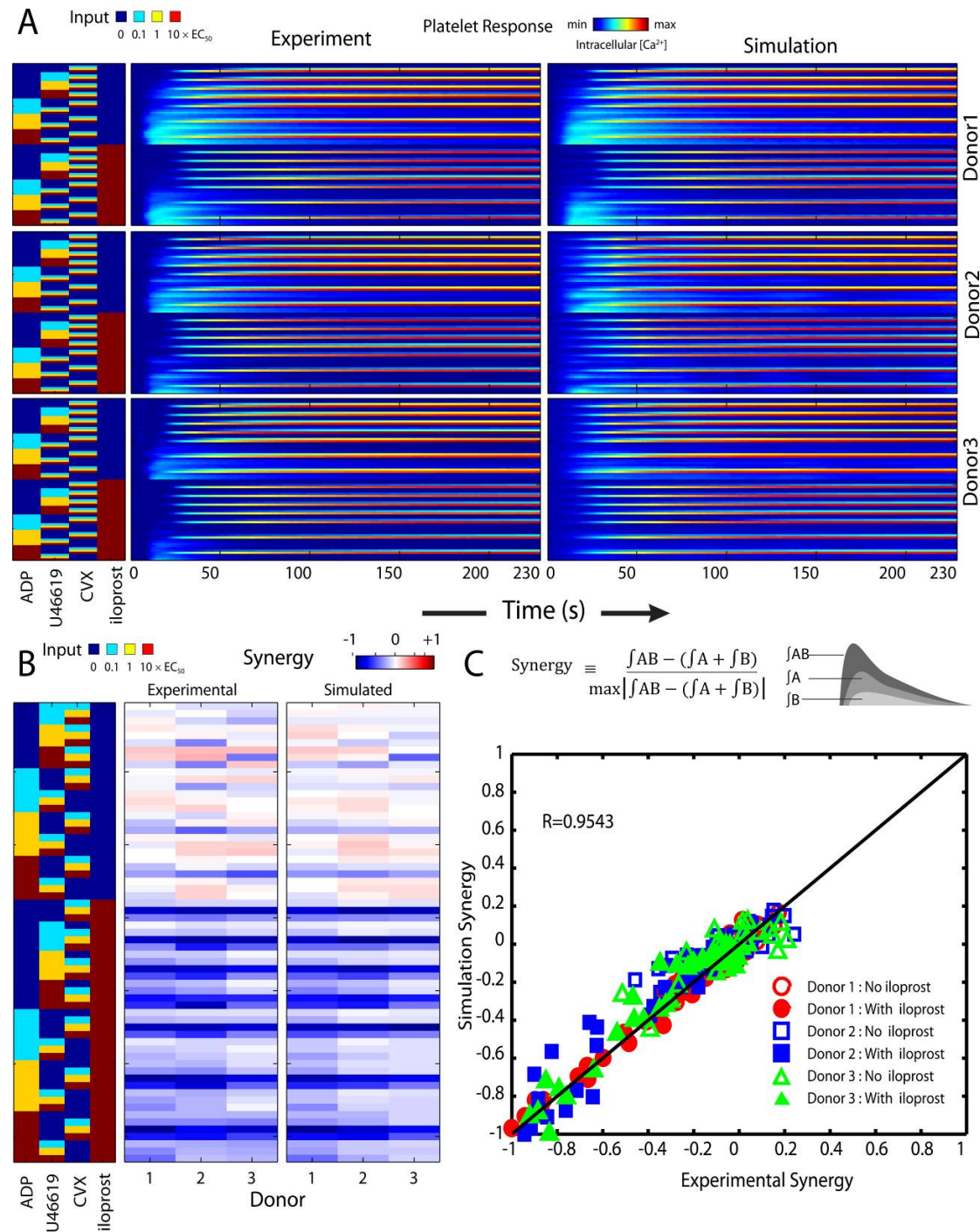


Flamm et al. *J. Chem. Phys.* 2009

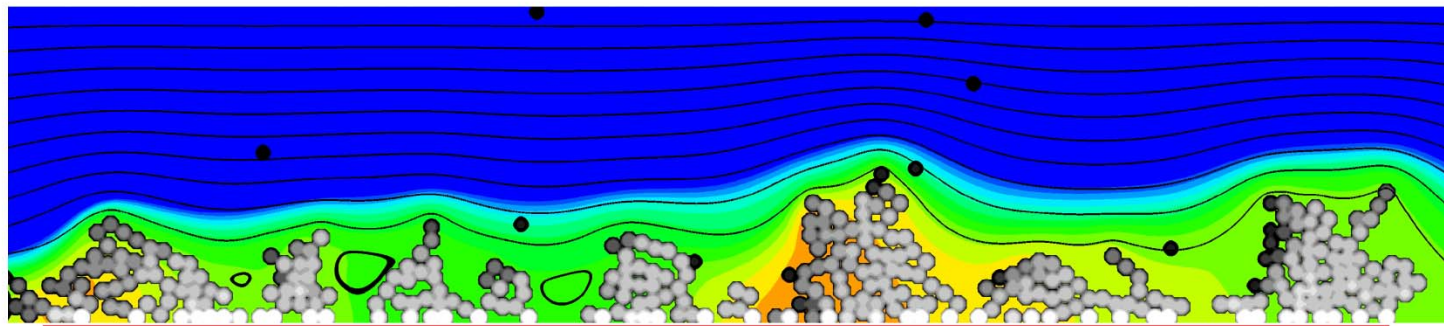
Flamm et al. *J. Chem. Phys.* 2011



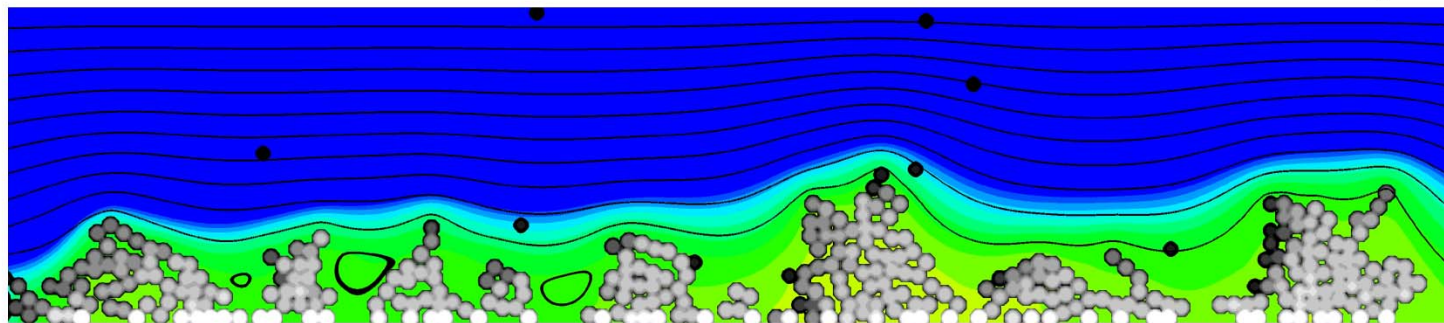
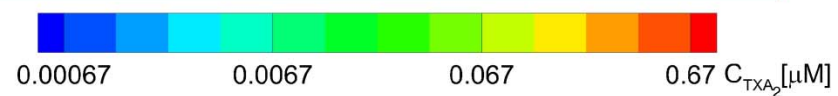
Flamm et al. *Blood*, 2012



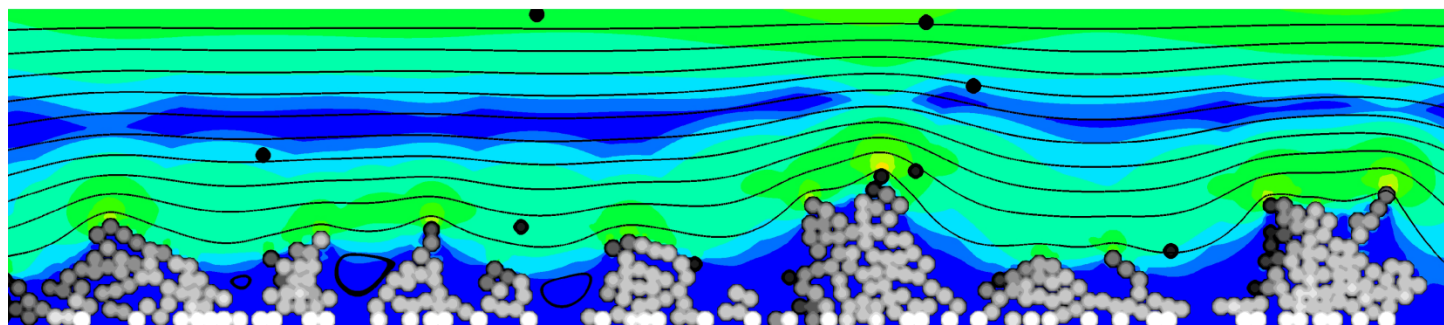
ADP



TXA₂



Shear Rate

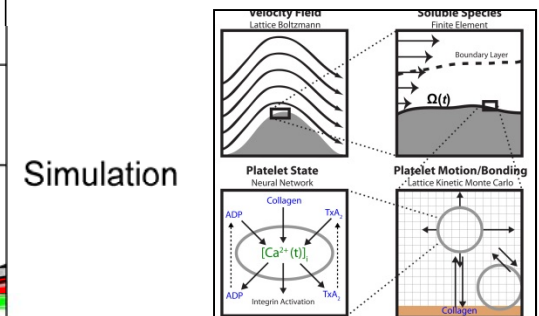
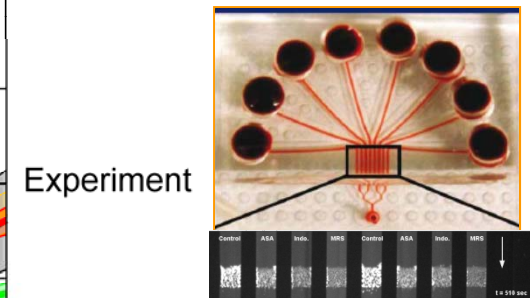
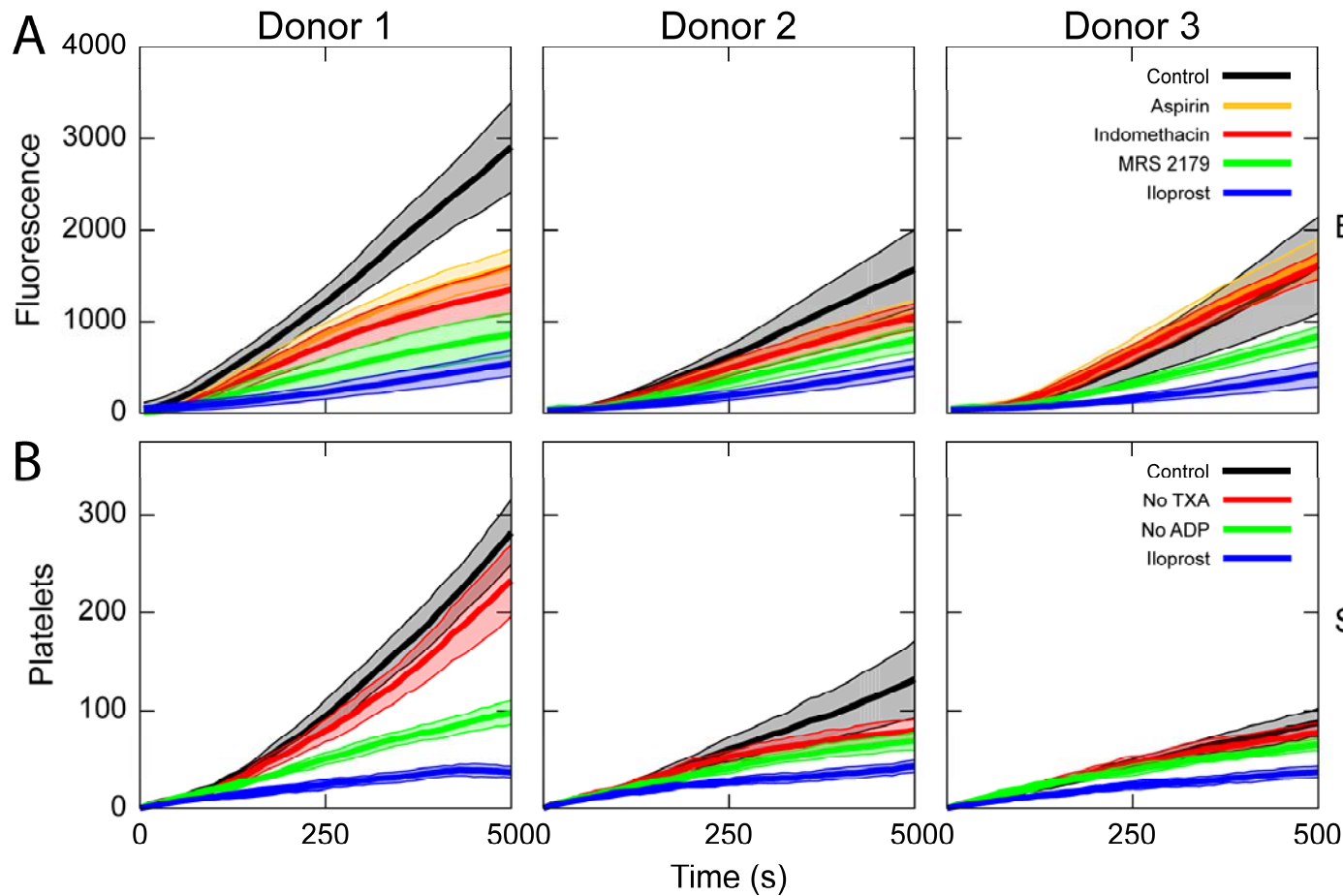


10 μ m

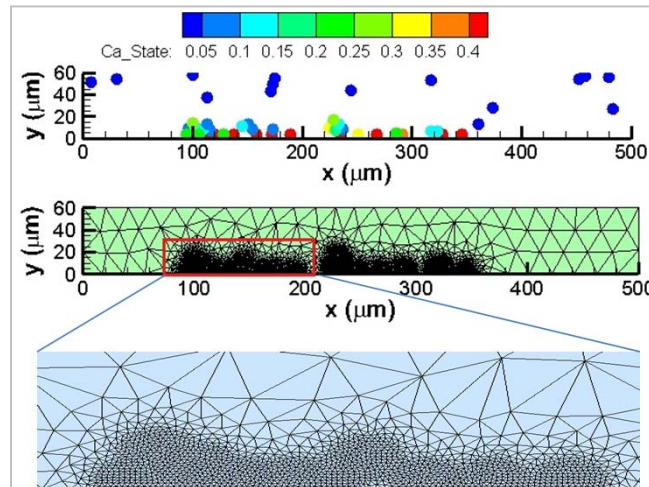
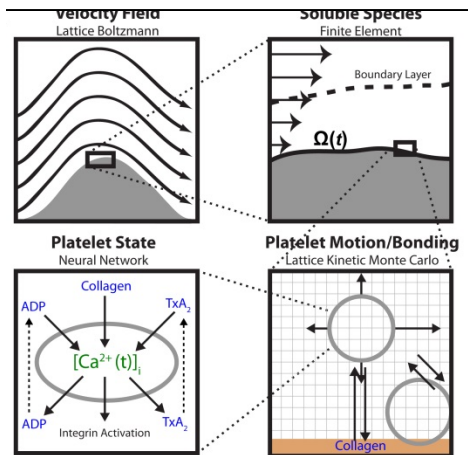
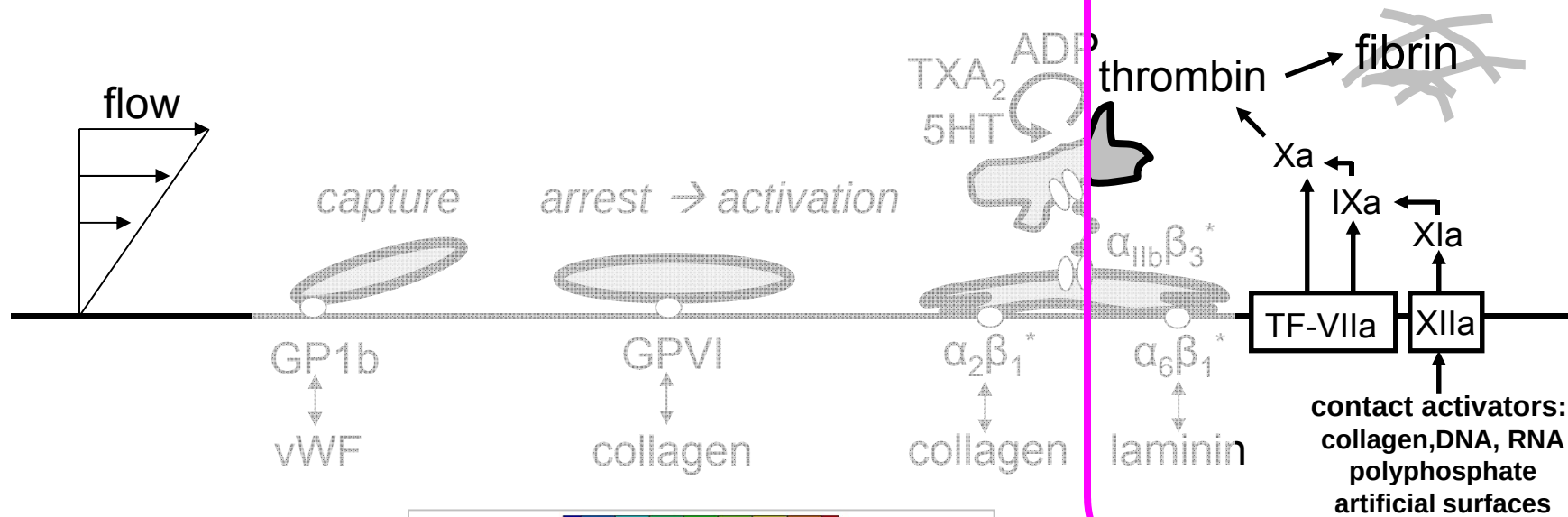
→ Flow



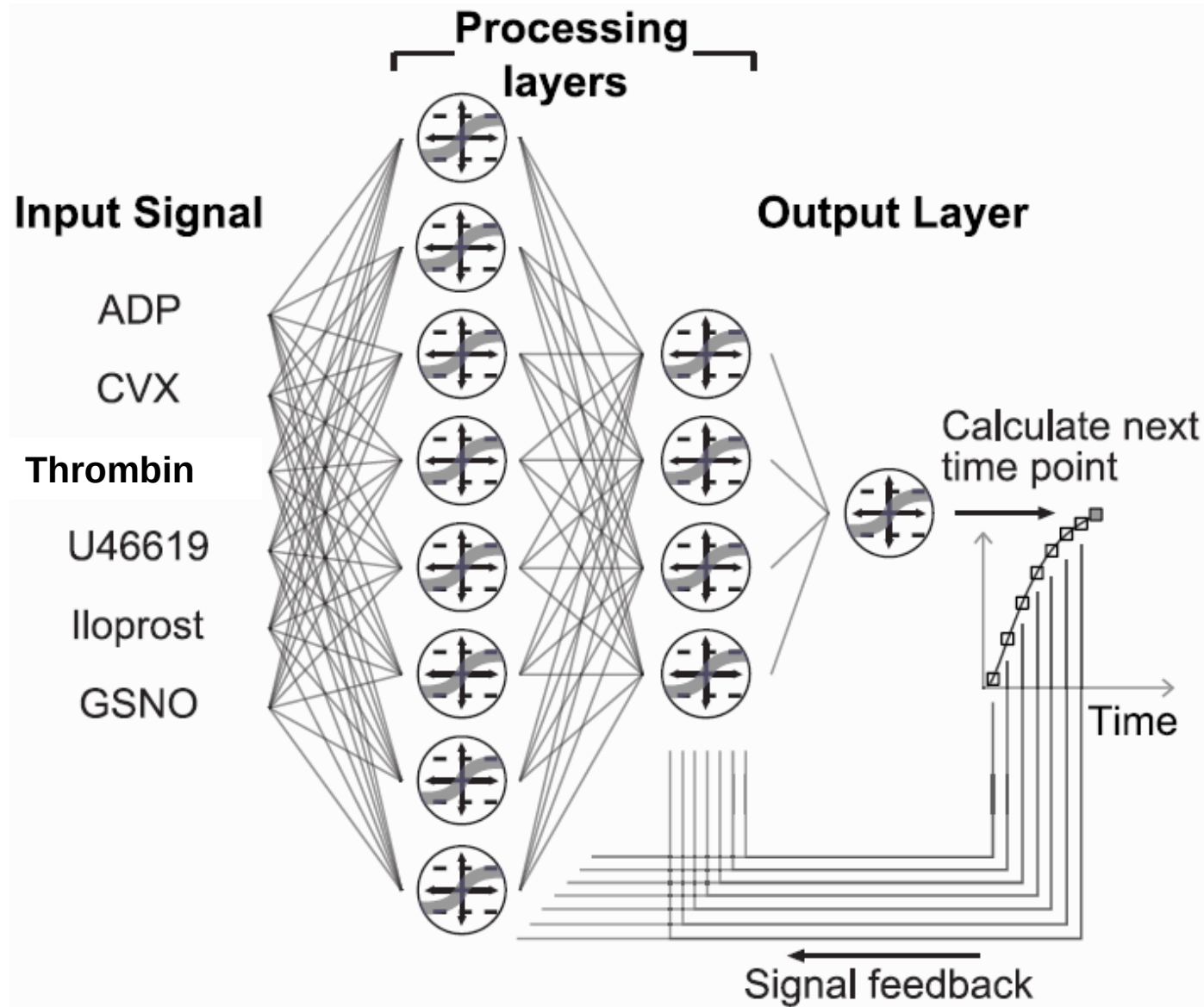
Microfluidic phenotyping of individual subjects (PPACK-whole blood over collagen 200 s⁻¹)



Platelet function during thrombosis and hemostasis

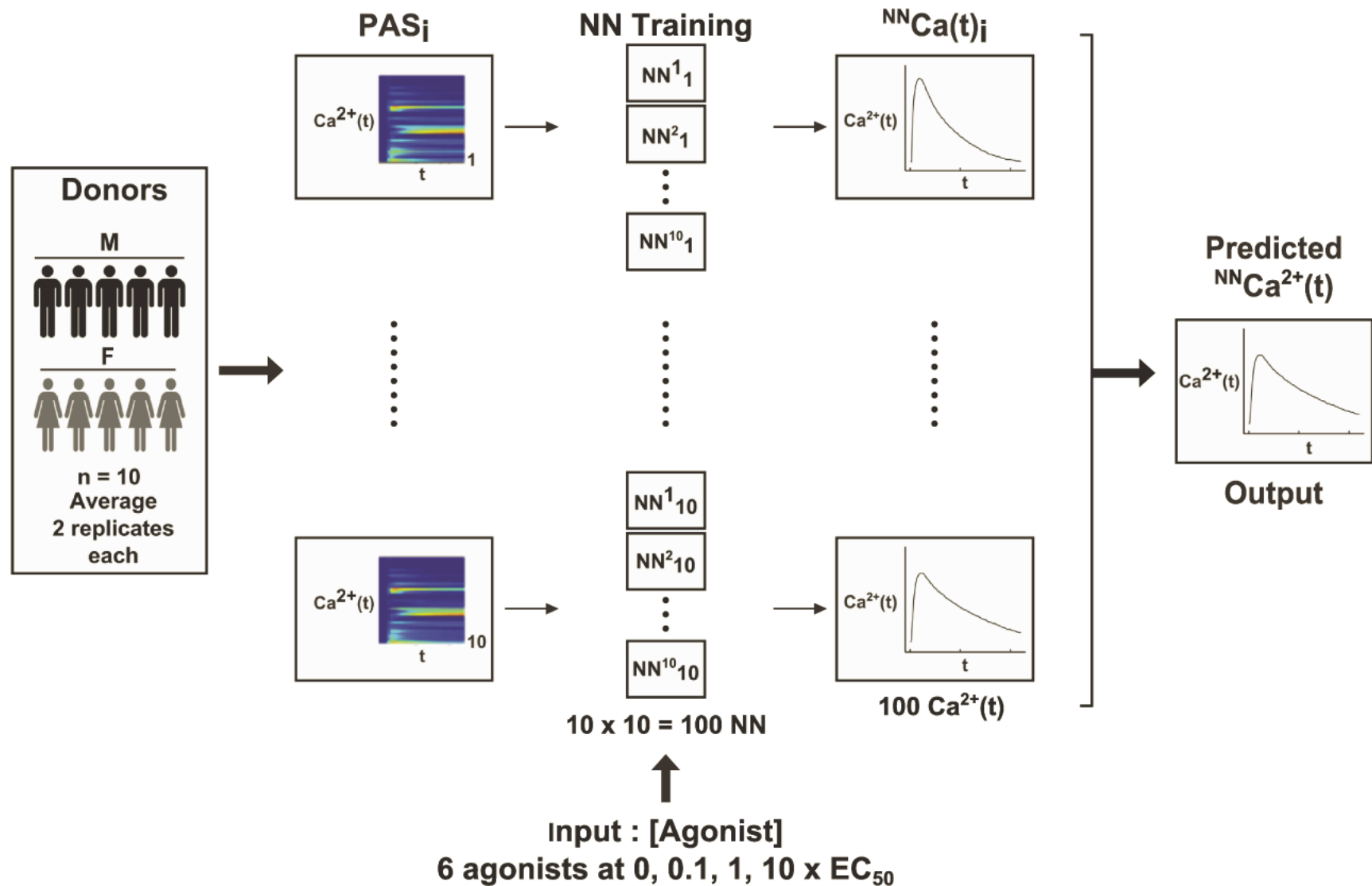


Neural Network Architecture

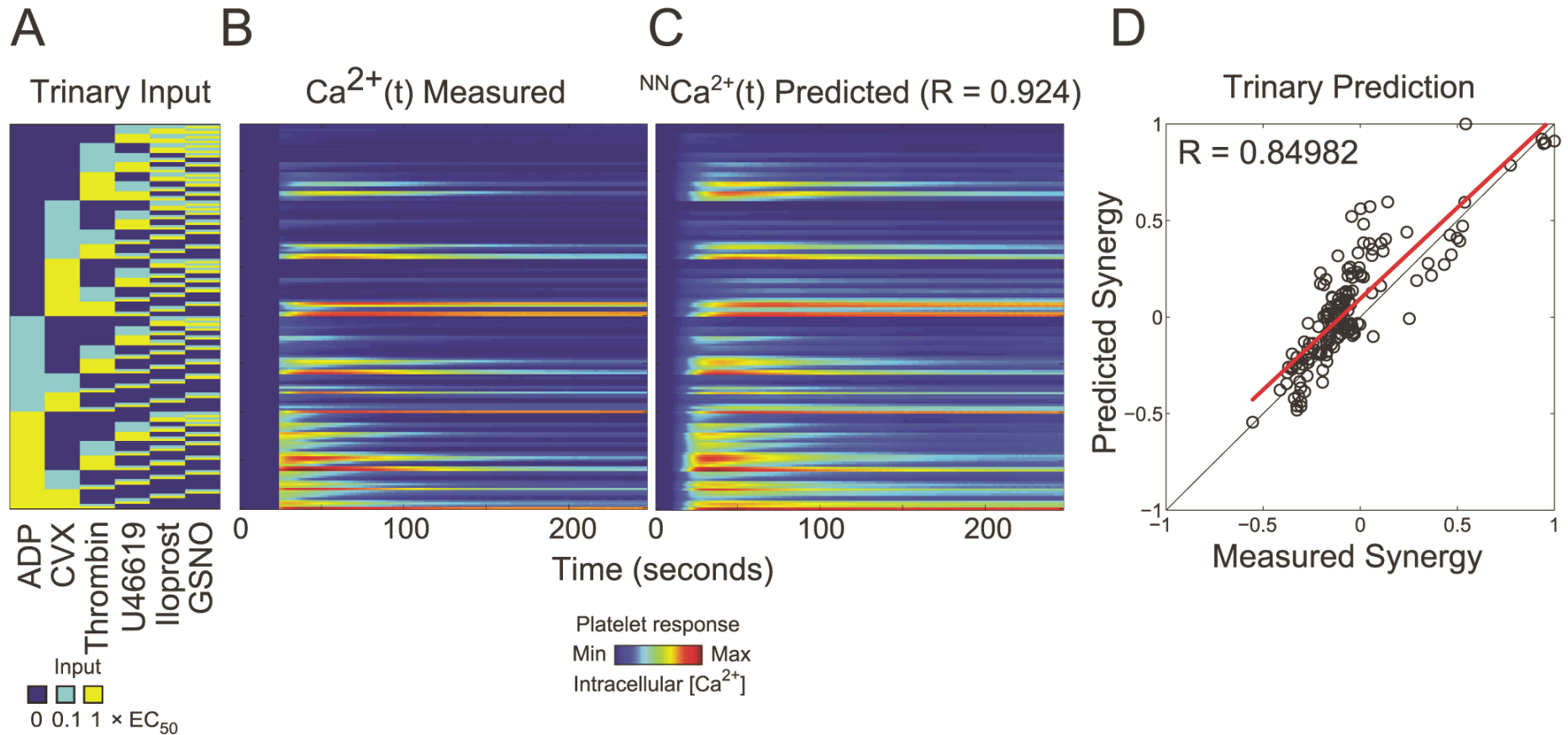


Lee et. al., PLOS Computational Biology., 2015

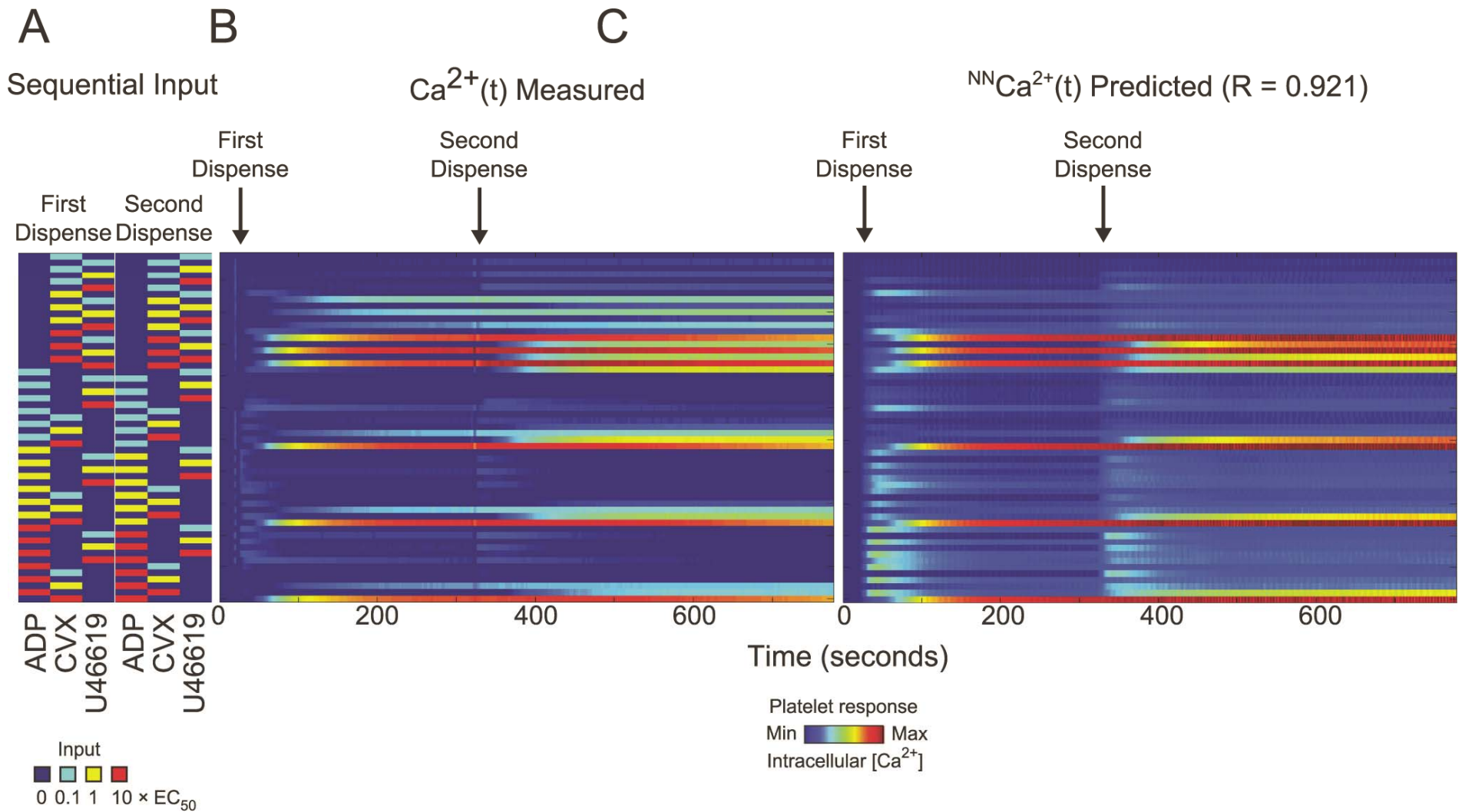
Neural Network Architecture

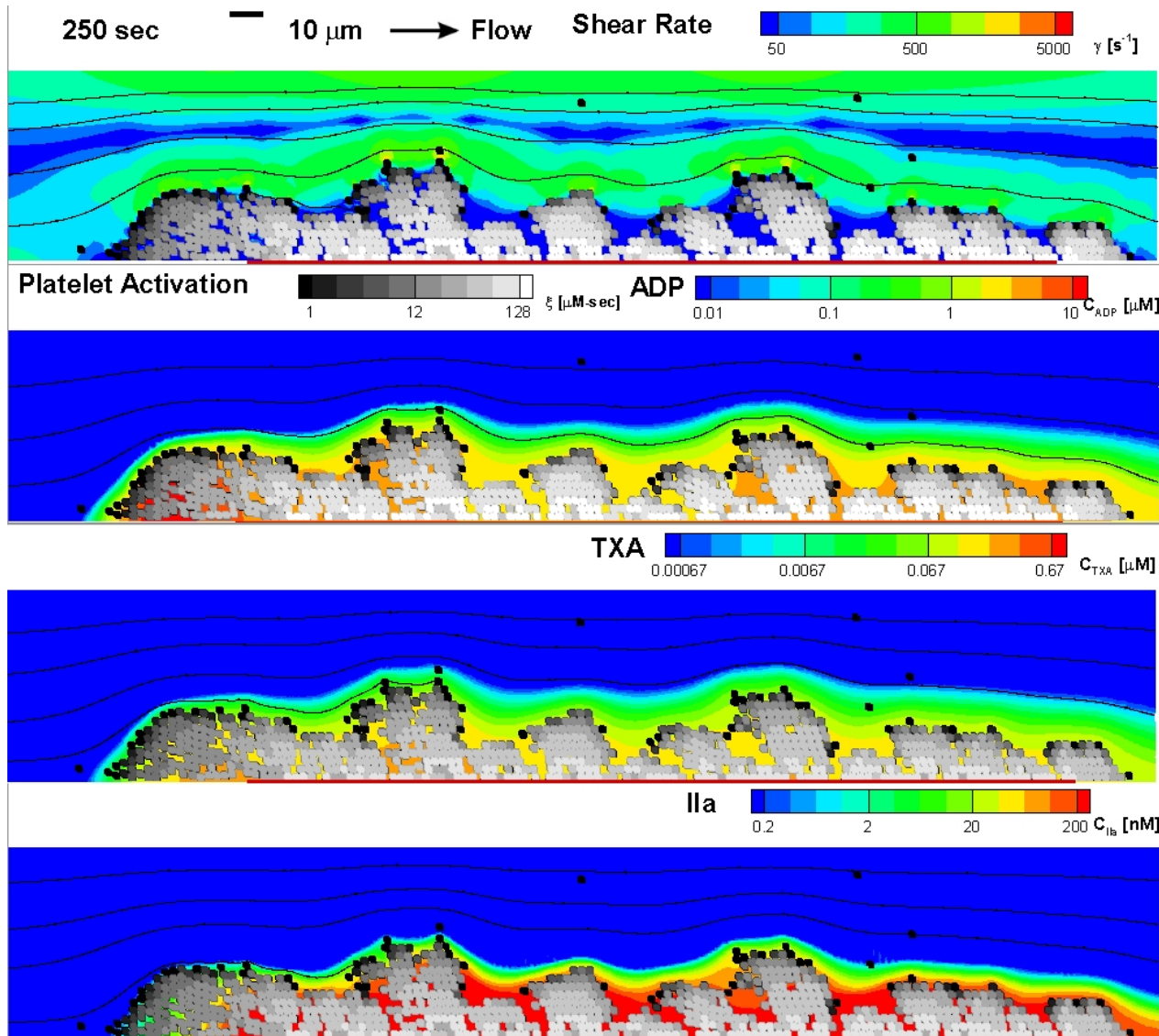


Trinary Predictions

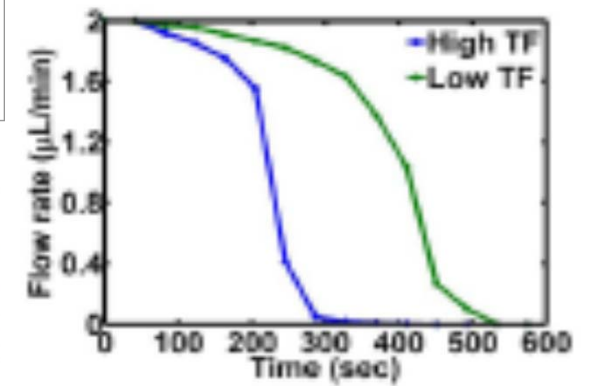


Sequential Exposures - Predictions

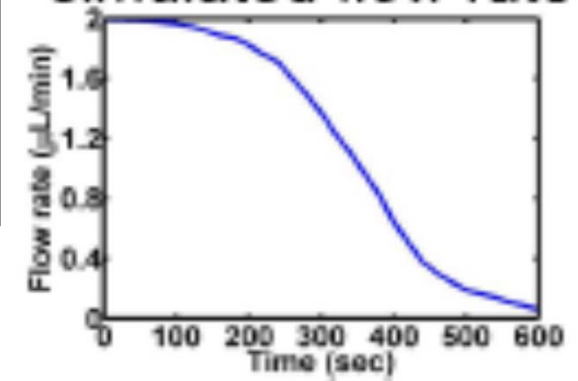




experimental flow rate

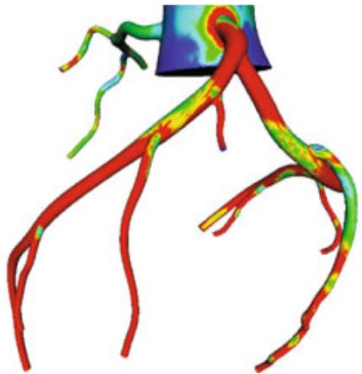
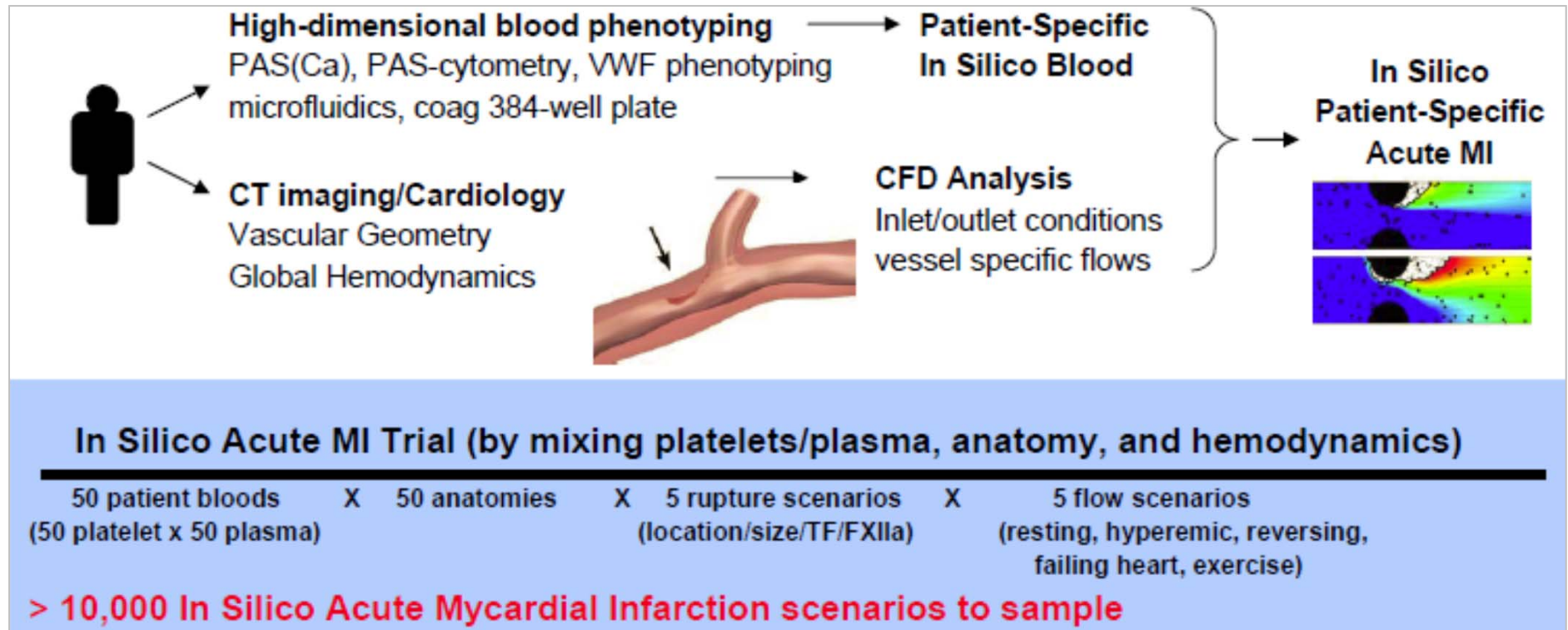


simulated flow rate



Future work: Diagnostics

– acute MI, trauma, hemophilia, neonatal, drug response



***Patient-specific Acute MI:
2D → 3D calculations,
Adaptive meshing, GPUs
Parallel processing***

